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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,561	05/02/2002	Dan L. Eaton	P3230R1C001-168	9766

30313 7590 08/23/2005

KNOBBE, MARTENS, OLSON & BEAR, LLP
2040 MAIN STREET
IRVINE, CA 92614

EXAMINER	
DUFFY, PATRICIA ANN	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 08/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,561	EATON ET AL.	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 May 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Sequence Attachments

DETAILED ACTION

The preliminary amendment filed 9-9-02 has been entered into the record. Claims 1-6 are pending.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 1-6 of this application.

According to the priority statement of 9/9/02, it appears that the claimed subject matter defined in the instant application is not supported by the parent application serial no. 10/006,867. Based on the information given by applicant and an inspection of the patent applications, the examiner has concluded that the subject matter defined in this application is not supported by the disclosure in any of the applications for which Applicants claim priority because the claimed subject matter does not have utility, enablement or written description in any of the prior applications for reasons set forth herein. Accordingly, the subject matter defined in claims 1-6 has an effective filing date of 5-2-02.

Should the applicant disagree with the examiner's factual determination above, it is incumbent upon the applicant to provide the serial number and specific page number(s) of any parent application filed prior to 5-2-02 which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of and fully enabled for prior to 5-2-02.

Drawings

The drawings in this application have been approved by the Draftsperson. No further action is required by Applicants.

Specification

The disclosure is objected to because of the following informalities:

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The title and abstract of the invention are not descriptive of the now claimed invention. A new title and abstract are required that is clearly indicative of the invention to which the claims are directed.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code at least at page 35. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Applicants should review the lengthy specification for other browser-executable code and delete or amend appropriately.

The use of the trademark ATCC™ has been noted in this application. They should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. For example, the trademark American Type Culture Collection (ATCC ™) needs to be recognized wherever it appears.

Information Disclosure Statement

The information disclosure statement filed 9-10-02 has been considered with the exception of the BLAST sequences. The BLAST results demonstrate that applicants are ware of nucleic acids with identity/homology to the one claimed herein. However, as the BLAST results do not give sufficient identifying information, the Examiner cannot determine if said sequences constitute prior art.

An initialed copy is enclosed.

Claim Objections

Claims 1-6 are objected to because of the following informalities: the claims improperly reference Figures. Referencing figures in a claim is only proper when the information contained therein cannot be represented in any other manner (MPEP 2173.05(s)). Further, the sequence rules require sequences to be claimed by their appropriate sequence identifier number and not Figure number. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

The pending claims have been reviewed in light of the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 USC 112, first paragraph, "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1092-111, Friday, January 5, 2001.

Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial and credible utility or, in the alternative a well-established utility.

The claims are drawn to antibodies that bind the polypeptide shown in Figure 52 (SEQ ID NO:52). The polypeptide is encoded by the polynucleotide of SEQ ID NO:51. The specification does not disclose any secondary or tertiary structural features of this polypeptide, nor does it assert that the polypeptide has any homology with known, characterized polypeptides. The instant specification does not disclose any additional information regarding PRO1411 such as biological activity, subcellular location, timing of regulation during cellular differentiation, which hormones or transcription factors regulate PRO1411, and what physiological significance PRO1411 plays. Therefore, it is a totally new, uncharacterized polypeptide with no well-established utility based on the above features of known characterized polypeptide families.

The specification generally asserts that all of the disclosed PRO polypeptides will be useful for a number of purposes; however, none of these asserted uses meet the three-pronged requirement of 35 U.S.C. § 101 regarding utility, namely, that the asserted utility be credible, specific and substantial. The asserted utilities will each be addressed in turn.

1) the PRO polypeptide or its antibodies can be used to isolate other polypeptides to which it binds: This asserted utility is not specific or substantial. Since the same can be done with any polypeptide, the asserted utility is not specific to the claimed PRO1411 polypeptides or antibodies thereto. Furthermore, since the specification does not disclose how PRO1411 or its binding partners can be used, significant further research would be required of the skilled artisan to determine how to use the claimed polypeptide or its binding partner. Since the asserted utility is not presented in a ready to use, real-world application, the asserted utility is not substantial.

2) the PRO polypeptide or its antibodies can be used as a molecular weight marker: This asserted utility is not specific. Since the same can be done with any polypeptide, the asserted utility is not specific to the claimed PRO1411 polypeptides or antibodies thereto.

3) the PRO polypeptide or its antibodies can be used in tissue typing: This asserted utility is not specific or substantial. With the exception of a few housekeeping genes, all polypeptides have a tissue specific pattern of expression, and thus virtually any polypeptide can be used in tissue typing. Thus, the asserted utility is not specific to PRO1411 of its antibodies.

4) the PRO polypeptide or its antibodies can be used in therapy in general: This asserted utility is not specific or substantial. Since a defect in any polypeptide is likely to cause a disease of some sort, every polypeptide is a target for drug development. Thus, the asserted utility is not specific to the claimed PRO1411 polypeptide or antibody. Furthermore, the specification does not disclose a nexus between any specific disease states and a change in amount or form of PRO1411. Significant further research would have to be conducted to identify such a nexus. Therefore, the asserted utility is not substantial.

5) the PRO polypeptide or its antibodies can be used to identify agonists or antagonists: Since the same can be done with any polypeptide, the asserted utility is not specific to the claimed PRO1411 polypeptides or antibodies. Furthermore, since no activity has been assigned to PRO1411, the assays cannot be conducted until the specific biological activities of PRO1411 are determined empirically. Therefore, the asserted utility is also not substantial.

6) the PRO polypeptide or its antibodies can be used in tumor/cancer diagnostics or therapeutics: The teaching of the specificaiton indicate that the polypeptide and antibodies thereto can be used in tumor/cancer diagnostics or therapeutics because the mRNA expression as assessed by quantitative PCR of cDNA libraries is "more highly expressed". In particular, the specification discloses that PRO1411 was tested using

quantitative PCR amplification reactions with cDNA libraries isolated from different human tumor and normal human tissue samples and analyzed by agarose gel electrophoresis so as to obtain a quantitative determination of the level of expression of the nucleic acid encoding the PRO polypeptide (specification page 140). The specification alleges that the differential expression in one or more tumor tissues as compared to one or more normal tissues of the same tissue type renders the molecule useful diagnostically for the determination of the presence or absence of tumor in a subject suspected of possessing a tumor as well as therapeutically as a target for the treatment of a tumor in a subject possession such a tumor. The specification lack utility for the protein and antibodies that bind it because (a) the higher levels of mRNA alleged in the specification have not been demonstrated to be statistically significant and (b) the art recognizes that neither gene copy number or mRNA levels predictably correlate with levels of protein expression. As to point (a) mRNA encoding the PRO1411 polypeptide (DNA 59212-1627) was reported as "more highly expressed in" normal skin as compared to melanoma tumor (see specification page 141). The specification is devoid of teaching of the number of samples tested, the statistical significance if any of the "more highly expressed" and the specific probe used for the alleged quantitative analysis performed. The data presented are not quantitative and as such, the relevance as compared to the recited control is ambiguous. Further, it appears that normal cells such as stomach and skin express the nucleic acid more highly as compared to tumors. As such, since the cDNA, proteins or antibodies are not described as being specifically correlated with a specific type of cancer the skilled artisan could not distinguish tumors from non-tumors based on the alleged "more highly expressed" criteria only. Therefore, the asserted use as diagnostic marker or targets of therapeutic intervention are not persuasive to impart a specific utility. This relevance of the asserted higher expression very vague, and does not disclose what mathematical calculations, if any, were used to establish significance of the finding across a variety of samples from different patients. Therefore, the apparent single data point presented in the

quantitative PCR is preliminary at best, and cannot be evaluated or repeated independently by the skilled artisan. Clearly, further research would be required of the skilled artisan to establish the statistical significance if any, and whether and how a probe used in the PCR assay could be used as diagnostic markers or therapeutic targets. Such further experimentation indicates that the asserted utility is not in currently available form for the disclosed nucleic acid of SEQ ID NO:51 encoding the polypeptide of SEQ ID NO:52. Furthermore, the literature indicates that such results are to be evaluated very critically. For example, Hu et al. (2003, Journal of Proteome Research 2:405-412) analyzed 2286 genes that showed a greater than 1-fold difference in mean expression level between breast cancer samples and normal samples in a microarray (p. 408, middle of right column). Hu et al. discovered that, for genes displaying a 5-fold change or less in tumors compared to normal, there was no evidence of a correlation between altered gene expression and a known role in the disease. However, among genes with a 10-fold or more change in expression level, there was a strong and significant correlation between expression level and a published role in the disease (see discussion section). Therefore, in the absence of a statistical significance of the data and quantitative evaluation it would appear that the relationship between the reported "higher expression" as it relates to tumor formation and role in tumor formation or role in normal cells remains to be established. Consequently, any relevance with respect to using the nucleic acid, protein or antibody for therapeutic purposes remains to be established. As to point (b), it is noted that the art establishes that increased mRNA production does not necessarily lead to increased protein production and hence the antibody cannot be predictably used for detection of increased polypeptide levels. Haynes et al. (Electrophoresis, 19:1862-1871, 1998) found "a general trend" but no significant correlation between nucleic acid level and translation and protein levels. Further, Haynes et al teach that polypeptide levels cannot be accurately predicted from mRNA levels and that variances as much as 40-fold or even 50-fold were not uncommon (p 1863). Haynes et al used yeast as an art-accepted model for eukaryotic

systems. Further, the lack of demonstrable correlation of mRNA expression levels with protein levels was so well known in the art at the time of filing, it was reported in a general text book. Lewin (Genes VI (1997) Chapter 29, pages 847-848) teaches that the concept that transcription levels do not correlate with protein levels was so well known to the art that it was presented in a textbook. Lewin, Genes VI (1997) Chapter 29, pages 847-848 which specifically teaches "... production of RNA cannot be inevitably be equated with production of protein...." (page 487, column 2, last paragraph . This concept reconfirmed by a variety of studies such as that evidenced by Gokman-Polar et al (Cancer Research 61:1375-1381, 2001) that indicates the absence of any necessary correlation between increased mRNA levels and increased protein levels. Gokman-Polar et al that teach "Quantitative reverse transcription-PCR analysis revealed that the PKC mRNA levels do not directly correlate with PKC protein levels, indicating that PKC isoenzyme expression is likely regulated at the posttranscriptional/translational level" (see abstract). Gokman-Polar et al show in Figure 6-7 that there is no increasing mRNA expression for any of the isoenzymes, while the protein is significantly overexpressed as shown by Figure 4-5. Anderson et al teach that "Despite extensive work on the regulation of many individual genes, little attention appears to have been paid to the global question of the relation between mRNA and corresponding cellular protein abundances.." (Anderson et al , Electrophoresis, 18:533-537, 1997; see page 536, column 2.). Anderson et al teach that the correlation is 0.48 and indicates that the two major phages of gene expression regulation are of approximately equal importance in determining the net output of protein. Reanalysis of the data of Kawamoto et al, indicates that the correlation is coefficient is poor when one gene product, well separated from the gene cluster is omitted from the calculation (Anderson et al page 536, column 2, first full paragraph). Further, the lack of correlation between mRNA levels and protein levels in cancer is demonstrated by Chen et al (Molecular and Cellular Proteomics, 1:304-313, April 2002). Chen et al indicate that "Using a quantitative analysis of mRNA and protein expression within the same lung

adenocarcinomas, we showed that only a subset of the proteins exhibited a significant correlation with mRNA abundance." (see Chen et al page 304, column 1, abstract). As such, not all cancer protein have a correlation and therefore, in the absence of any specific evidence to the contrary with respect to the polypeptide, variants thereof or antibodies that bind them, there is reason to doubt the asserted truth of the assertion of utility. Therefore, the skilled artisan immediately recognizes that, at the time of the invention, that no direct correlation between gene amplification/mRNA levels and increased polypeptide levels necessarily exists, no dogma exists between mRNA and polypeptide levels (for which neither are disclosed within the instant specification for polypeptide). Given the totality of the evidence provided by Haynes et al, Anderson et al, Chen et al and Lewin et al, it is clear that those skilled in the art would not assume that an alleged increase in gene copy number or increase in mRNA levels would correlate with increased polypeptide levels. One skilled in the art would have to do further research to determine whether or not the polypeptide levels were higher, and whether the higher levels were statistically significant. As such, the claimed antibodies that bind the polypeptides do not have utility.

Thus, the proposed use of the antibodies that bind PRO1411 polypeptides as diagnostic markers and therapeutic targets are simply starting points for further research and investigation into potential practical uses of the polynucleotides, encoded polypeptides and antibodies that bind the polypeptides. "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form- there is insufficient justification for permitting an application to engross what may prove to be a broad filed", and "a patent is not a hunting license". "[i]t is not a reward for the search, but compensation for its successful conclusion." Similarly, the other listed and asserted utilities in the specification as exemplified by the other

Examples are not particularly disclosed with respect to the claimed antibodies that bind polypeptides or are neither substantial nor specific due to being generic in nature and applicable to a myriad of such anti-polypeptide antibodies. (*Brenner v. Manson*, 148 USPQ 689 (Sus. Ct. 1996). Additionally, the courts have held that the disclosure is insufficient when testing is necessary to determine the actual use or possible lack of use (*In re Kirk and Petrow* (CCPA) 153 USPQ 48). Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility has not been assessed. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the nucleic acid per se, the polynucleic acid encoding the PRO polypeptide or the anti-PRO antibody that binds the polypeptide such that another non-asserted utility would be well established for the instantly claimed compounds.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 1 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites an antibody that binds a polypeptide, whereas claim 6 recites an antibody that *specifically* binds the same polypeptide. Neither the art nor the specification provide a clear definition for, or distinction between, "binds" and "specifically binds". Therefore, the metes and bounds of the claimed invention cannot be determined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Valenzuela et al (WO 99/55721, published 11-4-99).

Valenzuela et al teach a protein encoded by clone vd4_1 from human skin. The polypeptide is 85.1% identical as compared to SEQ ID NO:52 as set forth in the claims

and the protein of the prior art shows substantial regions of 100% identity (see attached sequence alignment). Valenzuela et al teach antibodies that bind the proteins produced by the clones. Valenzuela et al contemplate polyclonal, monoclonal, humanized, chimeric antibodies and fragments thereof (see pages 170, line 31 to page 172).

Claims 1-6 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Ruben et al (WO200061623, published 10-19-00).

Ruben et al teach a protein that is 85.9% identical as compared to SEQ ID NO:52 as set forth in the claims and the protein of the prior art shows substantial regions of 100% identity (see attached sequence alignment). Ruben et al teach polyclonal, monoclonal, chimeric, humanized, human antibodies and fragments thereof (see pages 186-195). Ruben et al teach that the antibodies maybe recombinantly fused or conjugated to molecules useful as labels in detection assays (page 191, lines 14-16).

Status of the Claims

Claims 1-6 stand rejected.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-

0855. The examiner can normally be reached on M-Th 6:30 am - 6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patricia A. Duffy, Ph.D.

Primary Examiner

Art Unit 1645

SEQUENCE ATTACHMENTS

GenCore version 5.1.6
Copyright (c) 1993 - 2005 Compugen Ltd.

OM protein - protein search, using sw model

Run on: June 22, 2005, 13:12:17 ; Search time 0.001 Seconds
(without alignments)
210.760 Million cell updates/sec

Title: us-10-063-561-52
Perfect score: 2363
Sequence: 1 MKFQGPLACLLLALCLGSGE.....KLGFINWDAINKDQRSSRIP 440

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 1 seqs, 479 residues

Total number of hits satisfying chosen parameters: 1

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : aay50941.geneseqp2000s:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	DB	ID	Description
1	2010.5	85.1	479	1	AAY50941	Human adult skin c

ALIGNMENTS

RESULT 1
AAY50941
ID AAY50941 standard; protein; 479 AA.
XX
AC AAY50941;
XX
DT 10-MAR-2000 (first entry)
XX
DE Human adult skin cDNA clone vd4_1 derived protein.
XX
KW Human; secreted protein; treatment; nutritional activity; cytokine;
KW cell proliferation; cell differentiation; hematopoiesis regulation;
KW tissue growth; activin; inhibin; chemotactic; chemokinetic; hemostatic;
KW thrombolytic; anti-inflammatory; invasion suppressor; tumor inhibition;
KW gene therapy.
XX
OS Homo sapiens.
XX
PN WO9955721-A1.
XX
PD 04-NOV-1999.
XX
PF 23-APR-1999; 99WO-US008504.
XX
PR 24-APR-1998; 98US-0082904P.
PR 11-JUN-1998; 98US-0088994P.
PR 12-JUN-1998; 98US-0089278P.
PR 02-JUL-1998; 98US-0091647P.
PR 24-AUG-1998; 98US-0097639P.
PR 22-APR-1999; 99US-00097639.
XX
PA (ALPH-) ALPHAGENE INC.
XX
PI Valenzuela D, Yuan O, Hoffman H, Hall J, Rapiejko P;
XX
DR WPI; 2000-052801/04.
DR N-PSDB; AAZ43803.
XX
PT New polynucleotides encoding secreted human proteins, derived from human
PT fetal brain, adult skin, adult brain, adult heart, adult thymus and adult
PT aorta cDNA libraries.
XX
PS Claim 63a; Page 255-256; 282pp; English.
XX
CC This invention describes novel human secreted proteins which are encoded
CC by polynucleotides obtained from fetal brain, adult skin, adult brain,
CC adult heart, adult thymus and adult aorta cDNA libraries. The
CC polynucleotides and proteins are predicted to have biological activities
CC which would make them suitable for treating, preventing or ameliorating
CC medical conditions in humans and animals, although no supporting data is
CC given. Suggested activities include nutritional activity, cytokine and
CC cell proliferation/differentiation activity, immune stimulating (e.g. as
CC vaccines) or suppressing activity, hematopoiesis regulating activity,
CC tissue growth activity, activin/inhibin activity,
CC chemotactic/chemokinetic activity, hemostatic and thrombolytic activity,
CC receptor/ligand activity, anti-inflammatory activity, cadherin/tumor
CC invasion suppressor activity, and tumor inhibition activity. The
CC polynucleotides are also stated to be useful for gene therapy. AAY50905-
CC Y50947 represent the secreted proteins described in the method of the
CC invention which are encoded by the polynucleotides represented in
CC AAZ43777-Z43808
XX
SQ Sequence 479 AA;

Query Match 85.1%; Score 2010.5; DB 1; Length 479;
Best Local Similarity 87.6%; Pred. No. 0;
Matches 380; Conservative 2; Mismatches 1; Indels 51; Gaps 2;

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Qy          1 MKFQGPLACLLLALCLGSGEAGPLQSGEESTGTNIGEALGHGLGDALSEGVGKAIGKEAG 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MKFQGPLACLLLALCLGSGEAGPLQSGEESTGTNIGEALGHGLGDALSEGVGKAIGKEAG 60

Qy         61 GAAGSKVSEALGQGTREAVGTGVRQVPGFGAADALGNRVGEAAHALGNTGHEIGRQAEDV 120
              |||||||||||||||||||||||||||||| ||||||||||||||||||||||||||||||
Db         61 GAAGSKVSEALGQGTREAVGTGVRQVPGFGVADALGNRVGEAAHALGNTGHEIGRQAEDV 120

Qy        121 IRHGADAVRGSWQGVPGHSGAWETSGGHGIFGSQGGLGGQGQGNPGGLGTPWVHGYPGNS 180
              ||||||||||||||||:||||||||||||||||||||||||||||||||||||||||||||
Db        121 IRHGADAVRGSWQGVPGHNGAWETSGGHGIFGSQGGLGGQGQGNPGGLGTPWVHGYPGNS 180

Qy        181 AGSFGMNPQGAPWGQGGNGGPPNFGTNTQGAVAQPGYGSVRASNQNEGCTNPPPSGSGGG 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 AGSFGMNPQGAPWGQGGNGGPPNFGTNTQGAVAQPGYGSVRASNQNEGCTNPPPSGSGGG 240

Qy        241 SSNSGGGSGSQSGSSGSGSNGDNNNGSSSGGSSSGSSSGSSSGGSSGGSSGGSSGNSGGS 300
              |||||||||||||||||||||||||||||||    ||||||||||||||||||||||||||
Db        241 SSNSGGGSGSQSGSSGSGSNGDNNNGSSSG----GSSSGSSSGGSSGGSSGGSSGNSGGS 296

Qy        301 RGDSGSESSWGSSTGSSSGNHGGSGGGNGHKPGCEKPGNEARGSGESGIQGFRGQGVSSN 360
              ||||||||||||||||||||||||||||||
Db        297 RGDSGSESSWGSSTGSSSGNHGGSGGGNGHKPG---------------------------- 329

Qy        361 MREISKEGNRLLGGSGDNYRGQGSSWGSGGGDAVGGVNTVNSETSPGMFNFDTFWKNFKS 420
                                  ||||||||||||||||||||||||||||||||||||||||
Db        330 --------------------GQGSSWGSGGGDAVGGVNTVNSETSPGMFNFDTFWKNFKS 369

Qy        421 KLGFINWDAINKDQ 434
              |||||||||||:|
Db        370 KLGFINWDAINKNQ 383
```

GenCore version 5.1.6
Copyright (c) 1993 - 2005 Compugen Ltd.

OM protein - protein search, using sw model

Run on: June 22, 2005, 13:11:14 ; Search time 0.001 Seconds
(without alignments)
170.280 Million cell updates/sec

Title: us-10-063-561-52
Perfect score: 2363
Sequence: 1 MKFQGPLACLLLALCLGSGE.....KLGFINWDAINKDQRSSRIP 440

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 1 seqs, 387 residues

Total number of hits satisfying chosen parameters: 1

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : aab38324.geneseqp2000s:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match %	Length	DB	ID	Description
1	2030	85.9	387	1	AAB38324	Human secreted pro

ALIGNMENTS

RESULT 1
AAB38324
ID AAB38324 standard; protein; 387 AA.
XX
AC AAB38324;
XX
DT 31-JAN-2001 (first entry)
XX
DE Human secreted protein encoded by gene 4 clone HKAJK47.
XX
KW Immunosuppressive; antiarthritic; antirheumatic; antiproliferative;
KW cytostatic; cardiant; vasotropic; cerebroprotective; neuroprotective;
KW nootropic; antibacterial; virucide; fungicide; opthalmalogical; human;
KW vulnerary; gene therapy; infection; secreted protein.
XX
OS Homo sapiens.
XX
PN WO200061623-A1.
XX
PD 19-OCT-2000.
XX
PF 06-APR-2000; 2000WO-US008979.
XX
PR 09-APR-1999; 99US-0128693P.
PR 26-APR-1999; 99US-0130991P.
XX
PA (HUMA-) HUMAN GENOME SCI INC.
XX
PI Ruben SM, Ni J, Komatsoulis GA, Rosen CA, Soppet DR, Shi Y;
PI Lafleur DW, Olsen HS, Ebner R, Florence KA, Moore PA, Birse CE;
PI Young PE;
XX
DR WPI; 2000-647418/62.
XX
PT New nucleic acid molecules encoding 62 human secreted proteins for
PT diagnosing, preventing, treating or ameliorating medical conditions and
PT used as food additives or preservatives.
XX
PS Claim 11; Page 593-595; 716pp; English.
XX
CC Sequences AAB38321-B38396 represent the amino acid sequences of 62 human
CC secreted proteins encoded by the genes AAC69512-C69587. The genes and
CC proteins are useful for preventing, ameliorating or treating medical
CC conditions, e.g. by protein or gene therapy. The genes are isolated from
CC a range of human tissues disclosed in the specification. The nucleic
CC acids, proteins, antibodies and (ant)agonists are useful in the
CC diagnosis, treatment and prevention of: (a) autoimmune diseases e.g.
CC rheumatoid arthritis; (b) hyperproliferative disorders e.g. neoplasms of
CC the breast or liver; (c) cardiovascular disorders e.g. cardiac arrest;
CC (d) cerebrovascular disorders e.g. cerebral ischemia; (e) angiogenesis;
CC (f) nervous system disorders e.g. Alzheimer's disease; (g) infections
CC caused by bacteria, viruses and fungi; and (h) ocular disorders e.g.
CC corneal infection. The polypeptides can also be used to aid wound healing
CC and epithelial cell proliferation, to prevent skin aging due to sunburn,
CC to maintain organs before transplantation, for supporting cell culture of
CC primary tissues, to regenerate tissues and in chemotaxis
XX
SQ Sequence 387 AA;

Query Match 85.9%; Score 2030; DB 1; Length 387;
Best Local Similarity 87.5%; Pred. No. 0;
Matches 385; Conservative 1; Mismatches 0; Indels 54; Gaps 2;

```
Qy          1 MKFQGPLACLLLALCLGSGEAGPLQSGEESTGTNIGEALGHGLGDALSEGVGKAIGKEAG 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MKFQGPLACLLLALCLGSGEAGPLQSGEESTGTNIGEALGHGLGDALSEGVGKAIGKEAG 60

Qy         61 GAAGSKVSEALGQGTREAVGTGVRQVPGFGAADALGNRVGEAAHALGNTGHEIGRQAEDV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 GAAGSKVSEALGQGTREAVGTGVRQVPGFGAADALGNRVGEAAHALGNTGHEIGRQAEDV 120

Qy        121 IRHGADAVRGSWQGVPGHSGAWETSGGHGIFGSQGGLGGQGQGNPGGLGTPWVHGYPGNS 180
              ||||||||||||||||||:||||||||||||||||||||||||||||||||||||||||||
Db        121 IRHGADAVRGSWQGVPGHNGAWETSGGHGIFGSQGGLGGQGQGNPGGLGTPWVHGYPGNS 180

Qy        181 AGSFGMNPQGAPWGQGGNGGPPNFGTNTQGAVAQPGYGSVRASNQNEGCTNPPPSGSGGG 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 AGSFGMNPQGAPWGQGGNGGPPNFGTNTQGAVAQPGYGSVRASNQNEGCTNPPPSGSGGG 240

Qy        241 SSNSGGGSGSQSGSSSGSGSNGDNNNGSSSGGSSSGSSSGSSSGGSSGGSSGGSSGNSGGS 300
              ||||||||||||||||||||||||||||||    ||||||||||||||||||||||||||||
Db        241 SSNSGGGSGSQSGSSSGSGSNGDNNNGSSSG----GSSSGSSSGGSSGGSSGGSSGNSGGS 296

Qy        301 RGDSGSESSWGSSTGSSSGNHGGSGGGNGHKPGCEKPGNEARGSGESGIQGFRGQGVSSN 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        297 RGDSGSESSWGSSTGSSSGNHGGSGGGNGHKPGCEKPGNEARGSGESGIQ---------- 346

Qy        361 MREISKEGNRLLGGSGDNYRGQGSSWGSGGGDAVGGVNTVNSETSPGMFNFDTFWKNFKS 420
                                                  ||||||||||||||||||||
Db        347 ------------------------------------NSETSPGMFNFDTFWKNFKS 366

Qy        421 KLGFINWDAINKDQRSSRIP 440
              ||||||||||||||||||||
Db        367 KLGFINWDAINKDQRSSRIP 386
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Search completed: June 22, 2005, 13:11:15
Job time : 0.001 secs